REMARKS/ARGUMENTS

I. SUMMARY

Claims 1 and 3-13 are pending and under examination in the present application. Claims 14-28 are pending, but withdrawn from consideration. Claims 1, 3-7 and 12-13 stand rejected under 35 U.S.C. §112, first paragraph. Claims 1 and 3-13 stand rejected under 35 U.S.C. §102(b) and §103(a). Applicants respectfully traverse each of these rejections and request the removal thereof based on reasons previously provided and Applicants' comments herein. Applicants submit that the present application is in condition for allowance and such action is earnestly solicited.

As a preliminary matter, Applicants note that the claim amendments herein do not affect the scope of the claims and are not intended to limit the claims in any way. The amendments are made to correct minor typographical errors and for consistency within the claims.

II. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1, 3-7, and 12-13 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled. Applicants respectfully traverse the rejection and request reconsideration and withdrawal of this rejection.

Applicants note that the Examiner's summary of the instant invention on page 2 of the Action is inaccurate, at least in that claim 1 has previously been amended, such that it now recites "...at least one mutated glucose/galactose binding protein having at least one substituted or added *cysteine group*; and at least one sensor surface wherein said mutated binding protein is coupled through said *cysteine group* to said surface..." [emphasis added].

The position that those skilled in the art would be unable to practice the invention without undue experimentation for all of the recited mutated binding proteins except for those shown in the figures, is without support and incorrectly attempts to shift the burden to Applicants. Indeed,

> "it is incumbent upon the Patent Office, whenever a rejection [based on lack of enablement] is made , to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up

> assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."

In re Marzocchi 439 F.2d 220, 224 (C.C.P.A. 1971) (first emphasis added). The Office Action, however, sets forth no reasons or evidence for the conclusive statement that those "skilled in the art would be unable to practice the invention as claimed without undue experimentation."

Applicants continue to assert and continue to present evidence that the claimed invention is not beyond the scope of the disclosure. By way of example, paragraphs 0008 and 0009 summarize the state of the art for the purposes of cysteine mutation in binding proteins and paragraph 0026 of the specification provides a list of over twenty example mutations of the GGBP protein having at least one substituted or added cysteine group. Paragraphs 0052-0059 of the specification also provide examples of methods for synthesizing mutated glucose/galactose protein. Furthermore, paragraphs 0060-0063 of the specification also provides examples of methods for immobilizing proteins onto a surface, and paragraphs 0064-0071 provide methods for detecting changes in refractive index for immobilized mutant proteins. In short, the specification provides a "considerable amount of guidance with respect to the direction in which experimentation should proceed." *In re Wands* 858 F.2d 731, 737 (Fed. Cir. 1988). Thus, the specification fully supports the entire scope of the claimed invention and demonstrates to those skilled in the art how to make and use mutated glucose/galactose binding proteins having at least one substituted or added cysteine group without undue experimentation.

In fact, the Examiner has acknowledged that at least one embodiment is fully enabled and that no undue experimentation is needed to practice the instant invention with respect to this enabled embodiment. *See Office Action*, page 3. And, as stated previously herein, the specification sets forth methods of detecting a signal based upon a change in refractive index of the claimed surface. In a similar set of circumstances, the Court of Appeals for the Federal Circuit, in overturning the district court's holding, held that a specification that supported one embodiment and also provided methods for determining activity (dose/response) fully enabled the claimed genus. *See United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1989). Applicants assert, therefore, that the specification fully enables the entire scope of the claimed invention.

For at least these reasons and the reasons Applicants have previously set forth in responding to this rejection under 35 U.S.C. §112, 1st paragraph, which are herby incorporated by reference, Applicants submit that the rejection is improper and should be withdrawn in its entirety. Such action is earnestly solicited.

III. REJECTION UNDER 35 U.S.C. § 102

Claims 1 and 3-13 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Lakowicz (US 6,197,534) or by Hellinga (US 6,277,627). Applicants respectfully traverse this rejection.

Neither Lakowicz nor Hellinga teach or suggest, among other things, the combination of the mutated binding protein and a sensor surface, as the claims require. Rather, all sensors disclosed in Lakowicz and Hellinga teach and require detection of glucose through a reporter group bound binding protein. ***The currently claimed invention does not require a reporter group, and a reporter group is not claimed.***

The Examiner also asserts that Lakowicz teaches a "sensor surface" (*Office Action*, page 5), but this characterization of Lakowicz is incorrect. Lakowicz teaches a ruthenium complex painted on the outside of a cuvette, with a binding protein in the cuvette, but not bound to any surface. In contrast, Applicants' claims recite a biosensor comprising at least one mutated binding protein and at least one *sensor surface*, wherein said mutated binding protein is *coupled* through said cysteine group *to said surface* where the sensor surface provides a signal resulting from a change in *refractive index*. The surface of the cuvettes in Lakowicz can not be used to detect chages in refractive index and can not be used as "sensor surfaces." Furthermore, the inner surfaces of the cuvettes in Lakowicz do not comprise binding proteins coupled thereto. Likewise, Hellinga does not mention or even suggest that binding proteins can be used in refractive index methods, as the current claims mandate. Applicants assert, therefore, that neither Lakowicz nor Hellinga can anticipate the claimed invention, because neither reference teaches or even suggests the combination of elements of the presently claimed invention. Reconsideration and withdrawal of the rejection are appropriate and respectfully requested.

IV. REJECTION UNDER 35 U.S.C. § 103

Claims 1 and 3-13 stand rejected under 35 U.S.C. §103(a), as allegedly being obvious over Lakowicz et al., (US 6,197,534) in view of Hellinga (US 6,277,627). Applicants respectfully traverse the rejection.

For at least the reasons indicated in prior responses and above with respect to anticipation, Applicants submit that no *prima facie* case of obviousness has been made. Additionally, Applicants submit that the claims are not obvious at least because: (1) the cited references alone or in combination do not teach *every* limitation of the currently claimed invention; (2) the Office Action has not shown that there is some suggestion or motivation in the references themselves, or within the knowledge of one of ordinary skill in the art, to alter or combine references to arrive at the claimed invention; and (3) the Office Action has not shown that there is a reasonable expectation of success in altering or combining the references.

As stated above with respect to anticipation, neither Lakowicz nor Hellinga teach the coupling of a mutant protein with the claimed surface sensor. In addition, both Lakowicz and Hellinga fail to teach detection of analyte binding by measuring changes in *refractive index*. Instead, Lakowicz and Hellinga each teach detection of analyte binding by measuring changes in *fluorescence*. Accordingly, the cited references do not teach *every* limitation of the currently claimed invention, and the claims are not obvious. In addition,

Additionally, the Office Action does not point to any motivation in Lakowicz or Hellinga to change the method of detection from fluorescence to refractive index. Because the references operate by fluorescence rather than by measuring refractive index, there is no motivation in the cited references to alter either to include a surface sensor at all, much less to immobilize mutated GGBP on a surface sensor. In fact, the Office Action can not possibly provide a suggestion or motivation to alter the teachings of Lakowicz or Hellinga to arrive at the claimed invention, because no such motivation exists. The Action makes the conclusory statement that modifying the references to provide a detectable signal from a change in refractive index is a "mere matter of judicious selection and routine optimization." There is no support in the Action for such a conclusion. Even if such a modification was within the capabilities of one skilled in the art, that is not sufficient to establish a *prima facie* case of obviousness. The Examiner must show that there is motivation to modify the references to establish a *prima facie* case, not merely that a

modification is capable of being made. See MPEP 2143.01. No motivation has been shown. Thus, for this reason as well, the claims are unobvious and the rejection should be withdrawn.

Moreover, the Examiner has not shown that there is a reasonable expectation of success in altering or combining the references. In fact, modification of Lakowicz as suggested by the Examiner may very well render the subject matter taught in these references inoperable for their intended purpose. For example, immobilization of mutated GGBP may affect the fluorescence measurements. Additionally, changing from the use of labeled binding protein to detect a fluorescence signal to immobilization on a sensor surface capable of providing a detectable signal resulting from a change in refractive index, completely changes the principle of operation of both cited references. Hellinga does not cure the fatal defects of Lakowicz, as both references are based on the use of fluorescence rather than refractive indices. Such a complete change in the principle of operation in Hellinga and Lakowicz is unobvious.

Because the Office Action has failed to meet all three criteria necessary to establish a *prima facie* case of obviousness, reconsideration and withdrawal of the rejection are appropriate and are again respectfully requested.

V. CONCLUSION

In view of the arguments presented, which are believed to obviate the outstanding rejections, Applicants respectfully request withdrawal of each rejection in its entirety and allowance of the present application.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he is invited to contact the undersigned at the telephone number listed below.

Atty. Dkt. No. P-5504
United States Serial No. 10/039,799

Respectfully submitted,

Date December 21, 2005

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